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=> d his ful

     (FILE 'HOME' ENTERED AT 18:12:29 ON 14 JUN 2006)

     FILE 'REGISTRY' ENTERED AT 18:12:36 ON 14 JUN 2006
L3             STR
L5              54 SEA SSS FUL L3

     FILE 'HCAPLUS' ENTERED AT 18:29:43 ON 14 JUN 2006
L8              19 SEA ABB=ON  PLU=ON  L5
L9            5968 SEA ABB=ON  PLU=ON  CONSTIPATION/CV OR INTESTINE, DISEASE (L)
                   CONSTIPATION/CV OR CONSTIPATION OR DEFECAT?
L10              1 SEA ABB=ON  PLU=ON  L8 AND L9
L11          45815 SEA ABB=ON  PLU=ON  (DEFECATION/CV OR ANTIDIARRHEALS/CV OR
                   DIARRHEA/CV OR FECES/CV OR LAXATIVES/CV) OR FECES OR ?LAXATIVE?
                    OR ?DYSCHEZ?
L13             18 SEA ABB=ON  PLU=ON  L8 NOT L10
L14            111 SEA ABB=ON  PLU=ON  "KAMEI K"/AU OR KAMEI KENSHI/AU
L15             35 SEA ABB=ON  PLU=ON  "SUDO H"/AU OR "SUDO HIROKAZU"/AU
L16            132 SEA ABB=ON  PLU=ON  "OZAKI KENICHI"/AU OR OZAKI K/AU
L17             42 SEA ABB=ON  PLU=ON  ("CYNSHI O"/AU OR "CYNSHI OSAMU"/AU)
L18            367 SEA ABB=ON  PLU=ON  "SATO HIDEKI"/AU
L19              0 SEA ABB=ON  PLU=ON  (L14 AND L15 AND L16 AND L17 AND L18) NOT
                   (L10 OR L13)
L20              1 SEA ABB=ON  PLU=ON  (L14 AND (L15 OR L16 OR L17 OR L18)) NOT
                   (L10 OR L13)
L21              0 SEA ABB=ON  PLU=ON  (L15 AND (L16 OR L17 OR L18)) NOT (L10 OR
                   L13)
L22              0 SEA ABB=ON  PLU=ON  (L16 AND (L17 OR L18)) NOT (L10 OR L13)
L23              0 SEA ABB=ON  PLU=ON  (L17 AND L18) NOT (L10 OR L13)
L24              0 SEA ABB=ON  PLU=ON  ((L14 OR L15 OR L16 OR L17 OR L18) AND (L9
                   OR L11)) NOT (L10 OR L13)

     FILE 'REGISTRY' ENTERED AT 18:48:39 ON 14 JUN 2006
L25         10070 SEA ABB=ON  PLU=ON  ERYTHROMYCI?

     FILE 'HCAPLUS' ENTERED AT 18:49:21 ON 14 JUN 2006
L26         22136 SEA ABB=ON  PLU=ON  L25 OR ?ERYTHROMYCI?
L27             0 SEA ABB=ON  PLU=ON  ((L14 OR L15 OR L16 OR L17 OR L18) AND
                   L26) NOT (L10 OR L13)
L29        173969 SEA ABB=ON  PLU=ON  (MACROLIDES/CV OR ERYTHROMYCIN/CV OR
                   "ERYTHROMYCIN A"/CV OR "ANTIBIOTIC RESISTANCE"/CV) OR MACROLID?
                    OR ANTIBIOTI?
L30             1 SEA ABB=ON  PLU=ON  ((L14 OR L15 OR L16 OR L17 OR L18) AND
                   L29) NOT (L10 OR L13)
L31             2 SEA ABB=ON  PLU=ON  L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR
                   L27 OR L30
                D STAT QUE L31
                D IBIB ABS HITSTR L31 1-2

     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:    13 JUN 2006  HIGHEST RN 887650-39-7
     DICTIONARY FILE UPDATES:   13 JUN 2006  HIGHEST RN 887650-39-7

     New CAS Information Use Policies, enter HELP USAGETERMS for details.
```

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 14 Jun 2006 VOL 144 ISS 25
FILE LAST UPDATED: 13 Jun 2006 (20060613/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 18:29:43 ON 14 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 14 Jun 2006  VOL 144 ISS 25
FILE LAST UPDATED: 13 Jun 2006  (20060613/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
L3                STR
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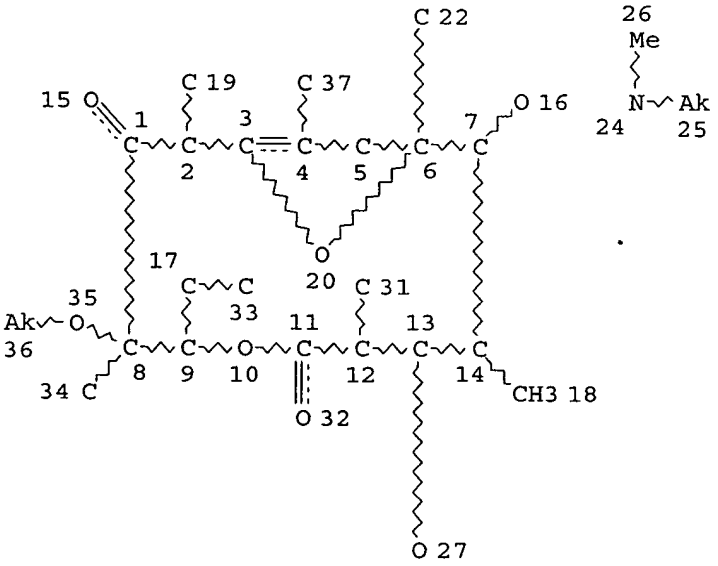


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  32
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STEREO ATTRIBUTES: NONE
L5            54 SEA FILE=REGISTRY SSS FUL L3
L8            19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L9          5968 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CONSTIPATION/CV OR INTESTINE,
                 DISEASE (L) CONSTIPATION/CV OR CONSTIPATION OR DEFECAT?
L10            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND L9


=>
=>

=> d ibib abs hitstr l10 1

L10  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:368938  HCAPLUS
DOCUMENT NUMBER:          140:368695
TITLE:                    Therapeutic and/or preventive agent for dyschezia
INVENTOR(S):              Kamei, Kenshi; Sudo, Hirokazu; Ozaki, Kenichi; Cynshi,
                          Osamu; Sato, Hideki
PATENT ASSIGNEE(S):       Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE:                   PCT Int. Appl., 29 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004037273         A1    20040506    WO 2003-JP13627         20031024
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2503088            AA    20040506    CA 2003-2503088         20031024
     AU 2003275652         A1    20040513    AU 2003-275652          20031024
     EP 1557169            A1    20050727    EP 2003-758879          20031024
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     US 2006014706         A1    20060119    US 2005-532585          20050425
PRIORITY APPLN. INFO.:                       JP 2002-311284      A   20021025
                                             WO 2003-JP13627     W   20031024

OTHER SOURCE(S):          MARPAT 140:368695
GI
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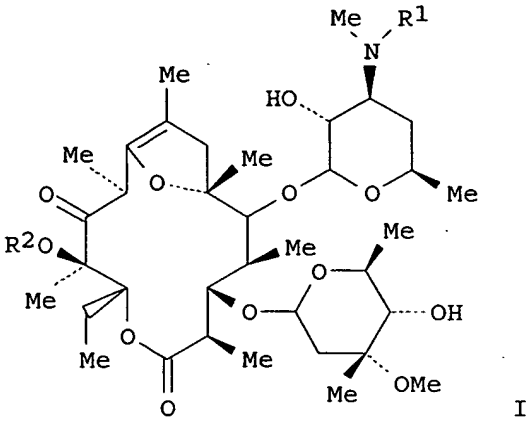
= inventive entity



I

AB A therapeutic and/or preventive agent for dyschezia which is suitable for persistent administration and contains as an active ingredient either a compound represented by the formula I (R1 and R2 = C1-6 alkyl) or a pharmaceutically acceptable salt of the compound The erythromycin derivative represented by the formula I functions to alleviate dyschezia. Unlike laxatives, the compound promotes natural **defecation.** The compound represented by the formula I has lower antibacterial activity than erythromycin and is hence suitable for long-term clin. use. Thus, the drug is safe and highly effective in treatments for and/or prevention of dyschezia.

IT **154802-96-7**, GM 611
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erythromycin derivative as a therapeutic and/or preventive agent for dyschezia)

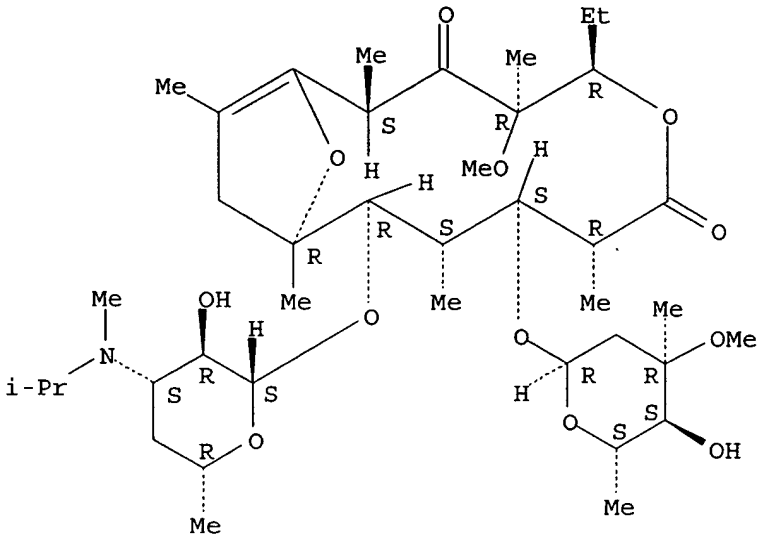
RN 154802-96-7 HCAPLUS

CN Erythromycin, 8,9-didehydro-N-demethyl-9-deoxo-6,11-dideoxy-6,9-epoxy-12-O-methyl-N-(1-methylethyl)-11-oxo-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 154738-42-8
CMF C40 H69 N O12

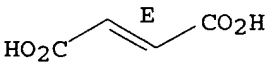
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => d stat que l13
L3 STR

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               L18) AND (L9 OR L11)) NOT (L10 OR L13)
L25        10070 SEA FILE=REGISTRY ABB=ON  PLU=ON  ERYTHROMYCI?
L26        22136 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 OR ?ERYTHROMYCI?
L27            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L14 OR L15 OR L16 OR L17 OR
               L18) AND L26) NOT (L10 OR L13)
L29       173969 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (MACROLIDES/CV OR ERYTHROMYCIN
               /CV OR "ERYTHROMYCIN A"/CV OR "ANTIBIOTIC RESISTANCE"/CV) OR
               MACROLID? OR ANTIBIOTI?
L30            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L14 OR L15 OR L16 OR L17 OR
               L18) AND L29) NOT (L10 OR L13)
L31            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 OR L20 OR L21 OR L22 OR
               L23 OR L24 OR L27 OR L30


=>
=>

=> d ibib abs hitstr l31 1-2

L31  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1999:819382  HCAPLUS
DOCUMENT NUMBER:          132:64107
TITLE:                    Preparation of cephem compounds as antibacterial
                          agents
INVENTOR(S):              Hanaki, Hideaki; Yamazaki, Hiroaki; Tsuchida, Yoshio;
                          Sato, Hideki; Hiramatsu, Keiichi; Kawashima,
                          Seiichiro
PATENT ASSIGNEE(S):       Zenyaku Kogyo K. K., Japan
SOURCE:                   PCT Int. Appl., 63 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 9967256            A1    19991229    WO 1999-JP3367          19990624
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
             JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2335768            AA    19991229    CA 1999-2335768         19990624
     EP 1090920            A1    20010411    EP 1999-926786          19990624
         R:  BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE
     AU 744164             B2    20020214    AU 1999-43927           19990624
PRIORITY APPLN. INFO.:                       JP 1998-177880      A   19980624
                                             WO 1999-JP3367      W   19990624

OTHER SOURCE(S):          MARPAT 132:64107
GI
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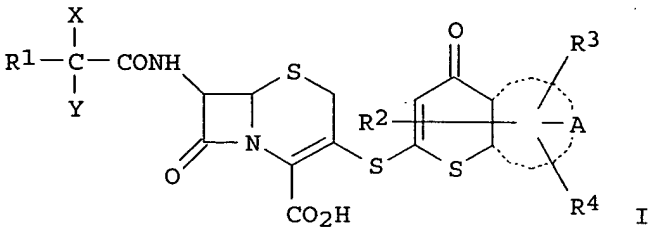
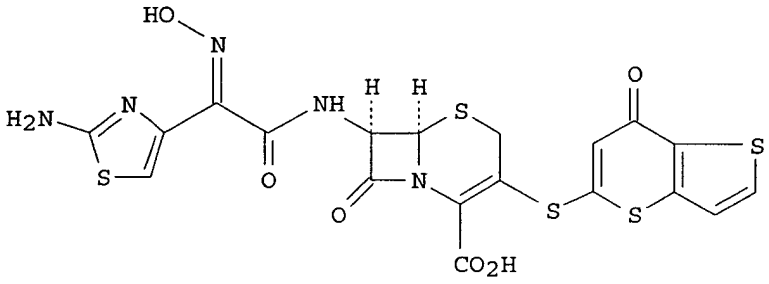


I



II

AB Cephem derivs. represented by general formula [I; wherein the ring containing A is a benzene ring, a pyridine ring, a pyrazine ring or a five-membered aromatic heterocycle (containing one oxygen or sulfur atom as the cycle-constituting atom); X and Y are each hydrogen, or alternatively CXY is C:N-OH; R1 is Ph, thienyl or thiazolyl (which may be substituted with amino or halogeno); and R2, R3 and R4 are each hydrogen, halogeno, hydroxy C1-C6 alkyl, isothiuronium C1-C6 alkyl, amino C1-C6 alkyl or amino C1-C6 alkyl thio Me, with the proviso that when the ring containing A is a five-membered aromatic heterocycle, R4 is absent] and pharmaceutically acceptable salts thereof are prepared These compds. exhibit antibacterial activity against methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus faecalis (VRE). Thus, benzhydryl 7β-amino-3-(7-oxo-7H-thieno[3,2-b]thiopyran-5-yl)thio-3-cephem-4-carboxylate was condensed with (Z)-2-trityloxyimino-2-(2-tritylaminothiazol-4-yl)acetic acid using dicyclohexylcarbodiimide followed by treatment with CF3CO2H and anisole to give title compound (II), which showed min. inhibitory concentration of 0.10, 1.56, and 0.78 μg/mL against S aureus FDA 209P, E. faecalis NCTC-12201, and MRSA as compared to 0.78, >1,000, and 1.56 μg/mL for vancomycin.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:26563 HCAPLUS

DOCUMENT NUMBER: 130:204891

TITLE: Hemodynamic and hormonal responses to nicorandil in a canine model of acute ischemic heart failure: a comparison with cromakalim and nitroglycerin

AUTHOR(S): Kamijo, Takeshi; **Kamei, Kenshi**; Sugo, Izumi; Kamiyama, Toru; **Sudo, Hirokazu**; Ohba, Yasuhiro

CORPORATE SOURCE: Fuji Gotemba Research Laboratories, Chugai Pharmaceutical Co., Ltd., Gotemba-shi, Shizuoka, Japan

SOURCE: Journal of Cardiovascular Pharmacology (1999), 33(1), 93-101
CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pharmacol. profiles of nicorandil in the cardiovascular system have been characterized by K-channel opening and nitrate activities. However, the effects of nicorandil on acute heart failure have yet to be elucidated. To investigate the effects of nicorandil under such pathophysiol. conditions, we administered nicorandil i.v. to dogs with acute ischemic heart failure induced by coronary embolization and compared the results with those induced by cromakalim and nitroglycerin. The heart failure in this experiment was demonstrated by a reduction of mean blood pressure (MBP) from 143 ± 3 to 129 ± 2 mm Hg ($p < 0.01$); cardiac output (CO) from 2.18 ± 0.10 to 1.06 ± 0.05 L/min ($p < 0.01$); stroke volume (SV) from 12.7 ± 0.6 to 6.8 ± 0.3 mL/min ($p < 0.01$); Vmax, an index of the contractility of the left ventricle, from 105.5 ± 4.4 to 49.9 ± 1.8 l/s ($p < 0.01$), and an increase in right atrial pressure (RAP) from 2.9 ± 0.3 to 5.3 ± 0.3 mm Hg ($p < 0.01$); left ventricular end-diastolic pressure (LVEDP) from 2.5 ± 0.4 to 26.0 ± 1.4 mm Hg ($p < 0.01$); and T, time constant of left ventricular relaxation, from 38.3 ± 0.8 to 62.4 ± 2.8 ms ($p < 0.01$). Furthermore, plasma renin activity (PRA) and plasma atrial natriuretic peptide (ANP) increased (from 1.72 ± 0.29 to 5.03 ± 0.68 ng AngI/mL/h, $p < 0.01$; from 103.9 ± 5.8 to 411.5 ± 29.4 pg/mL, $p < 0.01$, resp.), whereas brain natriuretic peptide (BNP) remained unchanged (from 23.1 ± 2.2 to 26.9 ± 1.4 pg/mL). Nicorandil (10-40 μg/kg/min, i.v. infusion for 20 min for each dosing) or cromakalim (0.25-1 μg/kg/min) decreased MBP, systemic vascular resistance (SVR), RAP, and LVEDP, and increased CO, SV, and Vmax. However, the reduction of RAP in cromakalim was significantly smaller than those of nicorandil and nitroglycerin in comparison at similar hypotensive doses. Nitroglycerin (2.5-10 μg/kg/min) decreased MBP, RAP, and LVEDP, and increased Vmax but did not change CO or SV. Increased plasma ANP levels, an index of cardiac filling pressure after induction of acute ischemic heart failure, were decreased significantly by cromakalim and tended to decrease by nicorandil or nitroglycerin. Plasma BNP levels and PRA were not influenced by any of these drugs. These results suggest that nicorandil produces the reduction of both preload and afterload followed by an improvement of cardiac contractility in this model. The increase in CO may be mediated mainly by the drug's K-channel opening activities and the reduction of venous tone by its nitrate properties. Nicorandil may prove to be useful in the treatment of acute ischemic heart failure.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

TITLE: 136:7
GM-611 (Chugai pharmaceutical)
AUTHOR(S): Peeters, Theo L.
CORPORATE SOURCE: Gut Hormone Laboratory, Louvain, B-3000, Belg.
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(4), 555-557
CODEN: COIDAZ
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. GM-611 is an erythromycin derivative that acts as an agonist at the motilin receptor. It is being developed by Chugai as a potential treatment for gastric motility disorder [169036], as well as reflux esophagitis, non-ulcer dyspepsia and diabetic gastroparesis [347963]. GM-611 is in phase II trials in the US for reflux esophagitis [322624], [347955], [399349]. GM-611 acts by a novel mechanism whereby it stimulates and promotes peristalsis in the stomach and other segments of the gastrointestinal tract [334994]. The drug was shown to produce a dose-dependent sustained depolarization of rabbit duodenal smooth muscle. Depolarization appeared to be associated with activation of monovalent cation-selective channels [273336]. In Dec. 2000, Credit Suisse First Boston predicted that successful development of GM-611 could lead to sales over $500 million [400228].

IT **154802-96-7**, GM 611
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GM-611 (Chugai pharmaceutical) for treatment of gastric motility disorder)

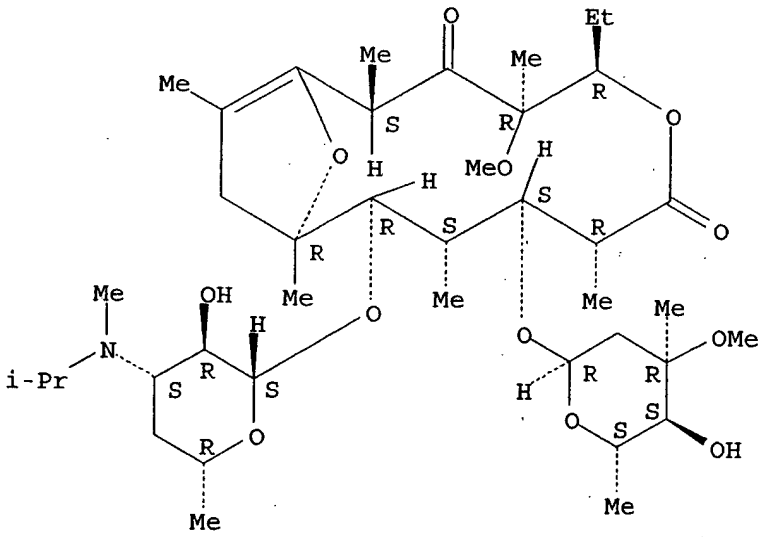
RN 154802-96-7 HCAPLUS

CN Erythromycin, 8,9-didehydro-N-demethyl-9-deoxo-6,11-dideoxy-6,9-epoxy-12-O-methyl-N-(1-methylethyl)-11-oxo-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 154738-42-8
CMF C40 H69 N O12

Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.